

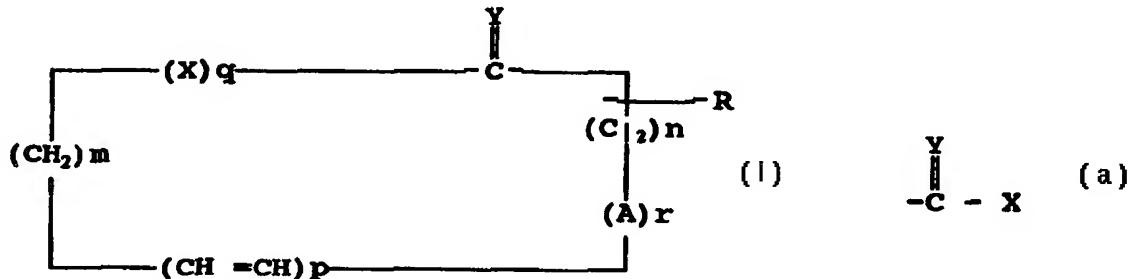


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(71) Applicants (for all designated States except US): CONREX PHARMACEUTICAL CORPORATION [US/US]; Kimberton Technical Center, Suite 120, 300 Kimberton Road, Phoenixville, PA 19640 (US). HSIEH, Phyllis (executrix for the deceased inventor) [US/US]; P.O. Box 326, Broadmore, PA 19316 (US).	
(72) Inventor: HSIEH, Dean (deceased).	Published <i>With international search report.</i>
(74) Agent: BARRON, Alexis; Synnestvedt & Lechner, 2600 Aramark Tower, 1101 Market Street, Philadelphia, PA 19107-2950 (US).	

(54) Title: COMPOSITION FOR ENHANCING SKIN OR HAIR



(57) Abstract

A composition and its use for enhancing the qualities of skin or hair, the composition comprising: (A) a skin-treating compound or a hair-treating compound; (B) an enhancer having structure (I) wherein: X and Y are oxygen, sulfur, or an imino group of the structure =N-R, with the proviso that when Y is the imino group, X is an imino group and when Y is sulfur, X is sulfur or an imino group; A is a group having the structure (a) wherein X and Y are defined; m and n are integers having a value of from 1 to 20 and the sum of m + n is not greater than 25; p is an integer having a value of 0 or 1; q is an integer having a value of 0 or 1; r is an integer having a value of 0 or 1; and R is hydrogen or an alkyl group having from 1 to 6 carbon atoms and may be straight chained or branched; with the proviso that when p, q and r have a value of 0 and Y is oxygen, m + n is at least 11; (C) a carrier; and optionally (D) a cosmetic additive.

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COMPOSITION FOR ENHANCING SKIN OR HAIRField of the Invention

This invention relates to means for improving a physiologic condition of the body. More particularly, this 5 invention relates to a composition which is effective in enhancing the qualities of skin or hair.

It is known that there are various types of materials which are effective in enhancing various properties of the skin, for example, properties such as smoothness of the skin 10 and texture of the skin. Examples of such materials are vitamins, anti-oxidants growth factors and steroids. Similarly, it is known that there are various types of materials which are effective in enhancing various properties of hair, including, for example, materials which function as 15 hair conditioners and materials which function to improve the manageability of hair.

The present invention relates to the provision of an improved composition for enhancing the qualities of skin or hair.

20

Summary of the Invention

In accordance with the present invention, there is provided a composition which is effective in enhancing the qualities of skin or hair and which comprises: (A) a skin-treating or hair-treating compound; (B) an enhancer, as 25 described below; (C) a carrier; and optionally (D) a cosmetic additive.

Another aspect of the present invention is the provision of a method for enhancing one or more properties of the skin or hair comprising applying to the skin or hair a composition

of the present invention. In preferred form, the composition is applied to the bodily part in the form of a cream or lotion.

Numerous benefits which are provided by the present
5 invention will be evident from examples set forth below.

Detailed Description of the Invention

As set forth above, the composition of the present invention comprises a skin- or hair-treating compound, an enhancer, a carrier, and optionally a cosmetic additive.

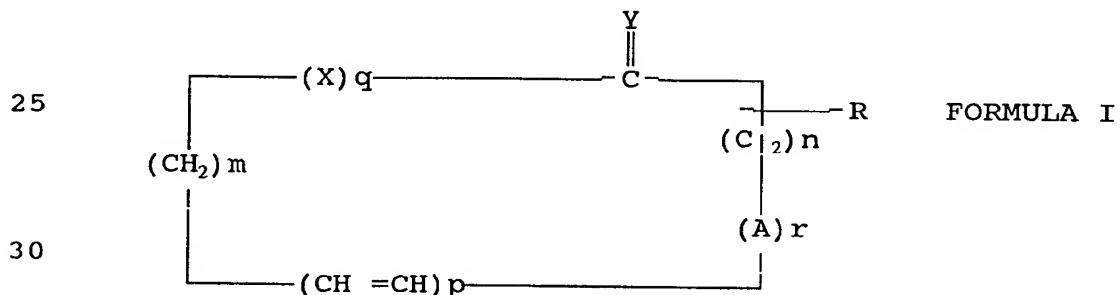
10 The term "skin-treating compound" means a material which is effective in enhancing one or more properties of skin as evidenced by statistically significant differences between the quality of untreated skin and skin treated with said material, at the 95% level of confidence, using standard
15 methods of evaluation which are known to persons skilled in the art. Examples of skin characteristics or properties that are capable of being improved by a skin-treating compound include: (A) smoothness of the skin; (B) thickness of the epidermal layer of the skin; (C) increase in the cellular
20 density of the skin; (D) reduction in the depth of interossei; (E) elasticity of the skin; and (F) texture of the skin. Methods for evaluating in an objective way skin properties of the aforementioned type are well known to persons skilled in the art. They include, for example, the
25 use of clinical assessments, photographic assessments, silastic castings, ultra-sound evaluation, histological examination, punch biopsies, and tape stripping.

Examples of classes of materials for use as skin-treating compounds in the practice of the present invention
30 include nutrients, modifiers, rejuvenators, hormones, regulators, immunomodulators, moisturizers, and stimulators. Examples of skin-treating materials for use in the practice of the present invention include: nutrients - vitamins, amino acids, and carbohydrates; modifiers - melanin and
35 antioxidants; rejuvenators - growth factors and human growth hormones; hormones - estrogens, progesterones and other steroids, and growth hormones; regulators - peptides, proteins, and anti-sense variations; immunomodulators - beta

1, 3-glucan and farnesol; moisturizers - vegetable oils, beeswax, and other waxes, lanolins, fatty acid esters, mineral oils, and other hydrophobic materials; and stimulators - tocopheryl nicotinate, retinoids, and alpha-5 hydroxy acids. A plurality of skin-treating compounds can be used in the composition.

The minimum percent improvement which is imparted by the skin-treating compound(s) to the skin and which constitutes a statistically significant difference, as referred to 10 hereinabove, will vary depending on the skin property being evaluated, as well as on sample size and distribution. For example, in evaluating epidermal thickness, an improvement of 10 % or greater is considered by persons skilled in the art as a statistically significant difference. On the other 15 hand, in evaluating elasticity of skin, an improvement of at least about 30 % would be considered by persons skilled in the art as constituting a statistically significant difference.

The skin-treating compound(s) is used in conjunction 20 with an enhancer which is a compound within the scope of Formula I below.



wherein: X and Y are oxygen, sulfur, or an imino group of the structure =N-R, with the proviso that when Y is the imino group, X is an imino group and when Y is sulfur, X is sulfur 35 or an imino group; A is a group having the structure $\begin{array}{c} Y \\ || \\ -C - X \end{array}$

wherein X and Y are defined; m and n are integers having a value of from 1 to 20 and the sum of m + n is not greater 40 than 25; p is an integer having a value of 0 or 1; q is an integer having a value of 0 or 1; r is an integer having a value of 0 or 1; and R is hydrogen or an alkyl group having

from 1 to 6 carbon atoms and may be straight chained or branched; with the proviso that when p, q and r have a value of 0 and Y is oxygen, m + n is at least 11. When R is alkyl, it can be, for example, methyl, ethyl, propyl, isopropyl, 5 butyl, isobutyl, sec - butyl, amyl, hexyl, and the like. A plurality of enhancers can be used. The enhancers for use in the practice of this invention are non-toxic and are compatible with skin/hair treating compounds which comprise the composition of this invention. Additional improvements 10 in the qualities of the skin are achieved by the use of the enhancer(s) in combination with the skin-treating compound. Such improvements are identified and evaluated by use of the same type of methodologies referred to hereinabove in connection with the skin-treating compound(s). 15 Preferably, the enhancer is a cyclic lactone compound wherein both X and Y are oxygen, q is 1 and r is 0, a cyclic diester (compounds wherein both X and Y are oxygen and both q and r are 1), and a cyclic ketone (compounds wherein both q and r are 0 and Y is oxygen). When the enhancer is a cyclic 20 diester, m+n is preferably at least 3. When the enhancer is a cyclic ketone, m+n is preferably from 11 to 15 and p is preferably 0. Particularly preferred enhancers for use of the practice of the present invention include macrocyclic ketones and lactones of Formula I above. A highly preferred 25 enhancer is cyclopentadecanolide.

The skin-treating compound or a mixture of skin-treating compounds should be used in an amount which is effective in improving the quality of the skin. The minimum amount(s) needed to achieve the improvement will vary depending on the 30 particular skin-treating compound or mixture of skin-treating compounds that are used. Generally speaking, it is believed that the skin-treating compound(s) will comprise at least about 0.01 wt.% of the composition. Typically, the skin-treating compound(s) will comprise about 0.1 to about 10 wt.% 35 of the composition. Preferably, the skin-treating compound(s) will comprise about 0.5 to about 3 wt.% of the composition.

The enhancer or a mixture of enhancers can be used in an amount at least effective to impart additional improvements

to the skin, that is, improvements beyond those provided by the skin-treating compound. It is believed that, for most applications, the enhancer will comprise about 0.1 to about 30 wt.% of the composition, with a preferred range of 5 enhancer being about 0.5 to about 10 wt.%, and a particularly preferred range comprising about 2 to about 5 wt.% of the composition.

The skin-improving composition of the present invention will generally include also a carrier in which the other 10 ingredients comprising the composition are either dissolved or dispersed in the form of solid particles or liquid droplets. Any suitable material can be used as the carrier, for example, materials which are suitable for use in pharmaceutical and cosmetic compositions. Examples of 15 carriers include water, alcohol, glycerine, sorbitol, propylene glycol, vegetable- and animal-derived oils, waxes, acids, alcohols, esters, ethers, amides, ethoxylates and propoxylates, ethylene and propylene glycol ethers, mineral oils and waxes, silicone oils and waxes, and surfactants. 20 The carrier can comprise one or more compounds. Speaking generally, the carrier will comprise about 10 to about 95 wt.% of the composition.

Optionally, but typically, the composition will include also one or more compounds which impart other desired 25 properties to the composition. Such compounds will typically comprise materials of the type that are used as additives in cosmetic compositions. Examples of such materials are fragrances, colorants, including pigments or dyes, preservatives, thickening agents, pH controlling agents, 30 stabilizers, surfactants, and emulsifiers.

The form of the composition can be liquid, semi-solid, or solid. The composition can be formulated so that it can be dispersed from an aerosol container. For convenience and ease of application, the use of the composition in a cream or 35 lotion form is recommended.

The skin-improving composition can be applied to the skin as often as needed to achieve the desired improvements. The frequency of application will vary depending on the nature of the composition and the involved skin condition.

In general, the application of the composition twice a day (for example, in the morning and the evening) will be suitable for treating many conditions and can be continued for as long as is required to obtain the desired results, for 5 example, weeks or months or indefinitely. For some conditions, the composition can be applied every two or three days. In treating the skin of the hands, consideration should be given to applying the composition after every washing.

10 Compositions for treating hair are also within the scope of the present invention. Such compositions can comprise hair-treating compounds, for example, materials which function as hair conditioners and compounds which improve the manageability of hair. Such compositions can comprise a 15 hair-treating compound and the enhancer of Formula I above, as well as other ingredients, and in amounts as described above in connection with the skin-improving composition.

It should be appreciated also that the enhancer of the present invention can be used to advantage in any type of 20 skin-enhancing composition which includes one or more skin-treating compounds that do not readily or easily penetrate the skin epithelial barrier. Such compositions are well known to those skilled in the art. An exemplary class of such compositions is an anti-oxidant composition. Such 25 compositions typically comprise a variety of natural nutrients, including, for example, vitamins, which function to rejuvenate the skin, retard the signs of aging of the skin and maintain the vitality of skin cells. In an in vivo comparative study involving the use of an anti-oxidant 30 composition within the scope of the present invention and Retin A, a material whose anti-wrinkle property has been well documented, it was determined that the performance of the composition of the present invention was equal to that of Retin A in terms of effecting an increase in epithelial 35 thickness, but without the side effects experienced with Retin A.

Examples 1 to 3 below are illustrative of anti-oxidant compositions which promote the natural repair process and retard aging of the skin by providing skin cells with

beneficial natural nutrients. The enhancer used in the compositions is cyclopentadecanolide. It is believed that the enhancer functions to aid in the delivery of the nutrients effectively to the skin cells for their nourishment. This results in rejuvenation of the skin, imparting to the skin a radiant and youthful appearance. The principal variations among the compositions are related to differences in viscosity and concentrations of ingredients. Such differences illustrate that the compositions can be tailor-made for ease and effectiveness of application - for example, for repetitive use during the day, especially after each time the body or parts of the body, such as the hands, are washed or otherwise cleaned, or for application at night prior to sleep.

15

Example 1 - Hand and Body Lotion

	Vitamin A Palmitate	0.38% w/w
	Magnesium Ascorbyl Phosphate	0.75
	Vitamin E Acetate	0.38
	Alpha-Bisabolol	0.38
20	Panthenol (Pantothenyl Alcohol)	0.25
	Edetate Disodium	0.10
	Sodium Citrate	0.60
	Trolamine (Triethanolamine)	1.70
	Diethanolamine Methoxycinnamate (DEA Methoxycinnamate)	2.00
25	Aloe Vera Gel Concentrate	1.00
	Beeswax, White	0.50
	Mineral Oil, Light	4.00
	Cetyl Palmitate	1.00
30	Soya Sterol	1.00
	Cetyl Alcohol	2.00
	Stearic Acid	3.00
	Carbomer 934	0.10
	Poly(Vinylpyrrolidone)/1-Eicosene Copolymer	1.00
35	Methylparaben	0.20
	Propylparaben	0.10
	Imidazolidinyl Urea (Imidurea)	0.30
	Butylated Hydroxytoluene (BHT)	0.20
	Cyclopentadecanolide	4.00
40	Fragrance	QS
	Water	QS
	Total	100.00% w/w

Example 2 - Hand and Body Cream

	Vitamin A Palmitate	0.50 w/w
	Magnesium Ascorbyl Phosphate	0.75%
	Vitamin E Acetate	1.50
5	Alpha-Bisabolol	1.00
	Panthenol (Pantothenyl Alcohol)	1.00
	Eddate Disodium	0.10
	Sodium Citrate	0.60
	Trolamine (Triethanolamine)	0.50
10	Diethanolamine Methoxycinnamate (DEA Methoxycinnamate)	2.00
	Aloe Vera Gel Concentrate	1.00
	Squalane	3.00
	Cetyl Esters	2.00
15	Stearyl Alcohol	4.00
	PEG-40 Stearate	4.00
	Glyceryl Monostearate	3.00
	Methylparaben	0.20
	Propylparaben	0.10
20	Imidazolidinyl Urea (Imidurea)	0.30
	Butylated Hydroxytoluene (BHT)	0.20
	Silicone Oils	5.50
	Cyclopentadecanolide	4.00
	Fragrance	QS
25	<u>Water</u>	<u>QS</u>
	Total	100.00% w/w

Example 3 - Night Cream

	Vitamin A Palmitate	0.375% w/w
	Magnesium Ascorbyl Phosphate	3.000
30	Vitamin E Acetate	1.500
	Alpha-Bisabolol	1.000
	Panthenol (Pantothenyl Alcohol)	1.000
	Eddate Disodium	0.100
	Sodium Citrate	0.600
35	Trolamine (Triethanolamine)	0.500
	Diethanolamine Methoxycinnamate (DEA Methoxycinnamate)	2.000
	Aloe Vera Gel Concentrate	1.000
	Squalane	3.000
40	Cetyl Esters	2.000
	Mineral Oil, Light	4.000
	Stearyl Alcohol	4.000
	PEG-40 Stearate	2.500
	Glyceryl Monostearate	4.500
45	Methylparaben	0.200
	Propylparaben	0.100
	Imidazolidinyl Urea (Imidurea)	0.300
	Butylated Hydroxytoluene (BHT)	0.200
	Silicone Oils	5.000
50	Cyclopentadecanolide	4.000
	Fragrance	QS
	<u>Water</u>	<u>QS</u>
	Total	100.00% w/w

The ingredients of the compositions of Examples 1 to 3 are formulated into a substantially homogeneous composition with standard mixing, stirring, or shearing equipment, including high shear, as well as motionless or other mixers, 5 for example, at room temperature - 90°C, to form a creamy emulsion or lotion with a smooth feeling. The resultant compositions can be packaged, as appropriate, in plastic or aluminum tubes, glass or plastic jars, or glass or plastic bottles. The compositions evidence gross physical stability 10 even under drastic conditions, for example, at 60°C for 3 months.

The hand and body cream of Example 2 is evaluated for effectiveness in tests involving humans (15 caucasians, aged 50 years and older). The test subjects use the composition 15 of Example 2 or a placebo cream, according to the blind code, for the first 2 months and then all subjects use the composition of Example 2. The test compositions are rubbed into the hands daily at night before the test subjects retire. The following techniques are used to evaluate the 20 performance of the composition on the back of the hand: (A) photographs; (B) silastic castings; (C) ultrasound B-mode scans; (D) biopsies for histological examination; and (E) ballistometry. The overall effects observed as a result of the use in the evaluations of the composition of Example 2 25 are summarized hereafter.

On the basis of photographic assessments (A) above, a comparison of the subjects shows a gradual improvement in the appearance of the dorsal surface of the hands as a result of the use of the composition of Example 2. Study of the 30 photographs reveal that there is a decrease in the number of lines, a decrease in the depth of the interossei, and a general improvement in the smoothness of the skin. Use of composition of Example 2 appears to improve both the quality of the stratum corneum and the hydration of the epidermis and 35 dermis. Improvement in the interossei depth, as manifested by a decrease in the depth, would indicate a dermal improvement.

Silastic castings of (B) above are evaluated and compared by two independent scorers. Changes in the skin's

topography are rated according to the following scale: positive response; no response or no change; and negative response or worsening. These results are then averaged. At 30 days, there is no significant difference in the skin's 5 topography. At 90 days, the silastic castings show that 60% of the subjects exhibited a positive response in the skin's topography, and at 180 days, 73% of the subjects have a positive response.

On the basis of ultrasound evaluation of (C) above, the 10 overall effects which are produced by use of the composition of Example 2 can be summarized by three observations: (1) the epidermis in most of the subjects becomes thicker and better hydrated; (2) the papillary dermis increases in density; and (3) the reticular dermis increases in density. The time 15 course of events shows a gradual increase in thickness and density to up to three or four months. After this period, the increase reaches a steady state or declines slightly. These findings suggest an initial proliferative effect of the product on the epidermis followed by dermal restructuring.

20 From histological examination of (D) above, the stained sections are examined and evaluated for the following parameters: (1) epidermal thickness; (2) size of the granular layer; (3) appearance of the stratum corneum; and (4) appearance of the dermis. Epidermal thickness increases by 25 19% over the course of the study, with a 50% increase being found in epidermal thickness in some subjects. Granular layer increases in all subjects to at least double in thickness. This increase is estimated by the number of granular cells. Stratum corneum appearance is markedly 30 different in most subjects. From a compacted initial appearance, the stratum corneum assumes a basket weave pattern that is associated with a younger epidermis. Dermal evaluation is difficult to assess in that no special stains are used. Overall most subjects will show an increase in 35 cellularity of the dermis. This finding would be consistent with a restructuring process of the dermis.

On the basis of ballistometer evaluation of (E) above, 10 subjects have a positive response and 4 subjects have no significant change. One subject has a negative response.

This test measures dermal changes (not epidermal changes) and suggests that some restructuring of the dermis is occurring.

Based on the data that is obtained in the evaluation of the use of the composition of Example 2, conclusions can be

5 made respecting the use of the composition of Example 2:

(1) the product is effective in increasing epidermal thickness; (2) the product is effective in producing a smooth, well structured stratum corneum; (3) the product increases epidermal proliferation; (4) the product increases 10 skin elasticity; (5) the product helps restore the dermal structure; and (6) the product is effective in restoring aging hands to a more youthful appearance.

The next two examples are illustrative of the use of the enhancer of the present invention in sunscreen compositions.

15 Such compositions typically contain a plurality of sunscreen agents which are compounds that function to protect the skin by virtue of their ability to absorb various wavelengths of potentially harmful ultraviolet radiation. Sunscreen compositions should have a combination of properties

20 including, for example: (A) the fundamental ability to absorb the involved radiation; (B) the ability to continue to absorb the radiation over a prolonged period of time; and (C) the ability to resist removal upon exposure to water and/or perspiration. It is known that various sunscreen agents

25 penetrate the skin relatively rapidly, with subsequent loss to lower skin layers (dermis) and eventually to systemic circulation. In the development of the present invention, it has been observed that the sunscreen agent(s) in the composition of the present invention is retained at higher

30 concentrations for longer periods of time in the epidermis.

It is believed that concentrating the sunscreen agent in the epidermis helps to provide a natural resistance to removal by exposure to physical contact and to water, including perspiration. The extent of this "retaining" effectiveness

35 is dependent on the particular sunscreen agent(s) and carrier used and the concentration of the enhancer. The enhancer used in each of the compositions of Examples 4 and 5 is cyclopentadecanolide.

Example 4 - Sunscreen Lotion

	Benzophenone-3 (Oxybenzone)	3.0% w/w
	Diethanolamine Methoxycinnamate (DEA Methoxycinnamate)	
5	Cyclopentadecanolide	3.0
	Silicone Oil	4.0
	Glyceryl Monostearate	5.0
	PEG-40 Stearate	5.0
	Sodium Lauryl Sulfate	1.0
10	Stearyl Alcohol	0.5
	Cetyl Esters	7.1
	Propylparaben	5.0
	Butylated Hydroxytoluene (BHT)	0.2
	Diethylene Glycol Monomethyl Ether	0.2
15	<u>Water</u>	30.0
	Total	<u>QS</u>
		100.0% w/w

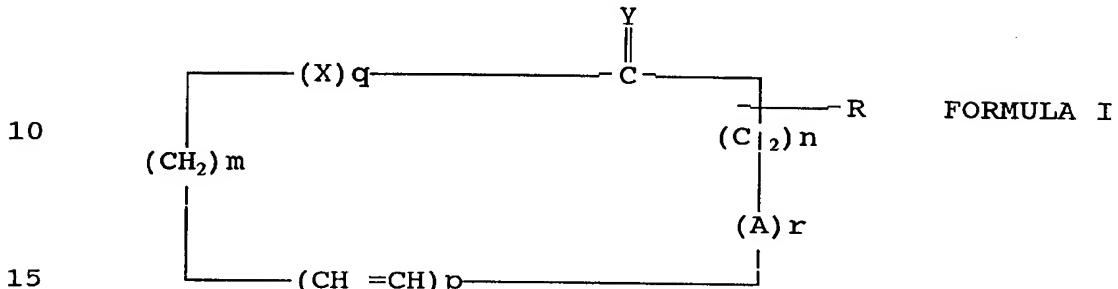
Example 5 - Sunscreen Lotion

	Benzophenone-3 (Oxybenzone)	3.00% w/w
	Diethanolamine Methoxycinnamate (DEA Methoxycinnamate)	
20	Cyclopentadecanolide	3.00
	Silicone Oil	4.00
	Glycerin (Glycerol)	1.00
	Propylene Glycol	5.00
25	Carbomer 941	5.00
	Squalane	0.25
	Stearic Acid	3.00
	Cetyl Esters	1.50
	Cetyl Alcohol	0.50
30	Glyceryl Monostearate	0.50
	PEG-40 Stearate	3.00
	Trolamine (Triethanolamine)	1.50
	Methylparaben	0.50
	Propylparaben	0.20
35	Imidazolidinyl Urea (Imidurea)	0.10
	Fragrance	0.30
	<u>Water</u>	<u>QS</u>
	Total	<u>QS</u>
		100.00% w/w

It should be appreciated that the present invention
40 provides an effective means for improving the delivery to the
body of a variety of types of materials which have beneficial
effects on the body.

Claims

1. A composition which is effective in enhancing the qualities of skin or hair and which comprises: (A) a skin-treating compound or a hair-treating compound; (B) an enhancer having the structure



wherein: X and Y are oxygen, sulfur, or an imino group of the structure =N-R, with the proviso that when Y is the imino group, X is an imino group and when Y is sulfur, X is sulfur or an imino group; A is a group having the structure

20

$$\begin{array}{c} Y \\ \parallel \\ -C - X \end{array}$$

wherein X and Y are defined; m and n are integers having a value of from 1 to 20 and the sum of m + n is not greater than 25; p is an integer having a value of 0 or 1; q is an integer having a value of 0 or 1; r is an integer having a value of 0 or 1; and R is hydrogen or an alkyl group having from 1 to 6 carbon atoms and may be straight chained or branched; with the proviso that when p, q and r have a value of 0 and Y is oxygen, m + n is at least 11; (C) a carrier; 25

30 and optionally (D) a cosmetic additive.

2. A composition according to Claim 1 wherein the amount of said compound in said composition is at least about 0.01 wt.%.

3. A composition according to Claim 1 comprising about 35 0.1 to about 10 wt.% of said compound and about 0.1 to about 30 wt.% of said enhancer.

4. A composition according to Claim 3 comprising about 0.5 to about 3 wt.% of said compound and about 0.5 to about 10 wt.% of said enhancer.

5. A composition according to Claim 3 comprising about 5 2 to about 5 wt.% of said enhancer.

6. A composition according to Claim 2 which is an anti-oxidant composition and wherein said compound includes an anti-oxidant material.

7. A composition according to Claim 1 wherein said 10 enhancer consists essentially of cyclopentadecanolide.

8. A composition according to Claim 2 wherein said enhancer consists essentially of cyclopentadecanolide.

9. A composition according to Claim 3 wherein said enhancer consists essentially of cyclopentadecanolide.

15 10. A composition according to Claim 4 wherein said enhancer consists essentially of cyclopentadecanolide.

11. A composition according to Claim 5 wherein said enhancer consists essentially of cyclopentadecanolide.

12. A composition according to Claim 6 wherein said 20 enhancer consists essentially of cyclopentadecanolide.

13. A composition according to Claim 1 including said skin-treating compound.

14. A composition according to Claim 7 including said skin-treating compound.

25 15. A composition according to Claim 13 in which the skin-treating compound includes a sunscreen agent.

16. A method for enhancing a property of the skin or the hair comprising applying thereto a composition of Claim 1.

17. A method according to Claim 16 including applying 5 to the skin a composition according to Claim 1 and including a skin-treating compound.

18. A method according to Claim 16 including applying to hair a composition according to Claim 1 and including a hair-treating compound.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/00154

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A61K 7/42, 7/44, 31/38, 31/335
US CL : 424/59, 60; 514/431, 450, 880, 946

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/59, 60; 514/431, 450, 880, 946

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,248,831 A (HOPP et al) 28 Sepetmber 1993, col. 5, lines 12-31.	1-15

 Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents:	
A document defining the general state of the art which is not considered to be of particular relevance	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
E earlier document published on or after the international filing date	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
O document referring to an oral disclosure, use, exhibition or other means	&* document member of the same patent family
P document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

07 MAY 1997

Date of mailing of the international search report

27 MAY 1997

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

JOHN W. ROLLINS

Telephone No. (703) 308-0196